metabolites of cytoxan and ifosfamide. These simulations include all 8 DNA central sequences that can support a 1-3 guanine-guanine crosslink (5'-GNC-3' and 5'-CNG-3' with N=A, T, G, or C) with both GC and AT-rich flanking sequences. These simulations show that the likelihood of forming an interstrand crosslink has a strong sequence preference for the 5'-GNC-3' orientation, in agreement with previous experiments and simulations. Additionally we find a slight dependence of the crosslinking efficiency on the intervening base. We also find that the distribution of crosslinking distances does not follow a simple normal distribution, but instead shows the presence of several DNA structural microstates with lifetimes of 10-100 ns. These simulations provide a basis for the design of new DNA-crosslinking drugs optimized for interstrand crosslinking.

1404-Pos Board B134
Characterization of DNA-CTAB Aggregates
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Oligonucleotides will aggregate in the presence of a surfactant, much like the DNA aggregates that form during the transportation of genes through cell membranes. Aggregates formed from oligonucleotides of 20 to 100 bases in length in the presence of the surfactant, CTAB (cetyl trimethylammonium bromide) have been characterized by UV spectroscopy and electrophoresis. UV spectroscopy showed that the absorbance increased as a result of light scattering from various sized aggregates that formed between oligonucleotides and CTAB when the ratio of CTAB to oligonucleotide concentration was about 0.5 or larger. Electrophoresis has been used to compare the mobilities of both single and double stranded DNA in the presence of CTAB. The results show that DNA - CTAB gives rise to smeared bands in the gels at room temperature indicative of a range of aggregate sizes where the aggregates may be falling apart as they migrate through the gel. Bands from gel electrophoresis of DNA-CTAB aggregates at 4° C do not appear smeared indicating that the presence of aggregates is temperature dependent. To better characterize these aggregates, we are currently staining the oligonucleotides with a fluorescent dye and visualizing them using microscopy and spectrofluorometry.

1405-Pos Board B135
Single Molecule Studies of Sequence Dependence Elasticity in DNA
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DNA looping is a vital regulatory process in the cell to maintain proper function and viability. In protein-mediated looping, the DNA's sequence dictates both protein binding sites and the local mechanical properties of the DNA. These mechanical properties, notably its elasticity and intrinsic curvature, govern the ease at which loops can form. To probe the effects of sequence dependence on elasticity and the loop formation process, single molecule experiments were performed on short segments (~150bp) of DNA with varying amounts of AT and GC content between the protein-binding operators. Tethered particle motion (TPM) microscopy was employed to observe protein-mediated DNA loop formation in this system, and an analytical model of the loop formation process was used to calculate the elasticity of the DNA from the observed loop formation rates. For comparison, axial constant-force optical tweezers were used to directly stretch the same DNA molecules mechanically to determine their persistence length as a measure for their elasticity. Our results indicate that the intraoperator sequence has a larger effect on elasticity in the loop formation experiments than in the stretching experiments, which we attribute to different elasticity regimes when the DNA is strongly bent as in a DNA loop, compared to the thermally induced small curvature fluctuations in stretched DNA.

1406-Pos Board B136
Mechanical Properties of DNA-Like Polymers
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This work continues to probe the mystery of what balance of forces creates the extraordinary mechanical stiffness of DNA to bending and twisting. In particular, we have been trying to understand the extent to which the charge of DNA contributes to stiffness through electrostatic stretching forces. Remarkably, neither theory nor experiment has resolved this issue over six decades. We have approached the problem by making a family of double-helical DNA-like polymers in which one of the four normal bases is replaced with an anionic, cationic, or neutral analog that alters canonical stacking, charge, or both. The resulting DNA-like polymers were characterized in a variety of ways, including determining bend stiffness using cyclization kinetics and atomic force microscopy experiments. Recent theory predicts that the variants with different charge densities should have dramatically altered bending rigidity. Remarkably, we show that these DNA-like polymers have bend stiffness within the range of reported values for sequence-dependent variation of the natural DNA bases. On the other hand, DNA twist flexibility was strikingly different among the polymers. These results suggest that electrostatic stretching forces do not contribute measurably to DNA bend stiffness, showing the inadequacy of recent theory and the need for new concepts.

1407-Pos Board B137
Investigating the DNA Folding Mechanics of Protamine
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In spermatogenesis, an arginine-rich protein called protamine ultimately replaces ~85 percent of the histones that bind DNA. After replacement, the protamine proteins cause folding of the DNA into a series of toroids, which allow for a high level of DNA compaction. This replacement and compaction 1) reduces the head size of the sperm to enhance their hydrodynamicity, 2) decreases the likelihood of DNA damage, and 3) removes the epigenetic markers passed on through histone modifications. Yet, little is known about the exact mechanism of protamine-induced DNA folding. Here, we measure DNA compaction using a tethered particle motion assay which allows us to measure folding without applying any external forces. In a tethered particle motion assay, a micron-sized bead is tethered to the surface via a DNA molecule. During DNA folding, the end-to-end length of the DNA decreases, decreasing the motion of the bead. When we measured the motion of the bead in the presence of low protamine concentrations (1 μM) we observed discrete changes in the DNA length that occurred in ~200 nm increments. We interpret these length changes as sequential looping of the DNA into a toroid. Interestingly, the first step in the looping appears to be reversible while subsequent steps are not, possibly due to inter-loop protamine interactions. We then calculate the energetics for the looping and compare our findings to current models. Our results show how protamine is able to fold DNA into a super-compacted state necessary for efficient sperm delivery, which provide novel insights into such limiting case in epigenetics.

1408-Pos Board B138
Measuring Energetics of Sharp DNA Bending from Breakage Kinetics of Small DNA Loops
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Double-stranded DNA (dsDNA) can undergo diverse modes of conformational changes inside a cell. Among them, dsDNA bending is closely associated with genome packaging and gene regulation, and therefore a consistent polymer model of dsDNA bending is essential for quantitative description of genome-related processes. The behavior of dsDNA at large length scales can be well described as a worm-like chain whose bending energy depends quadratically on curvature. However, many studies on dsDNA bending at short length scales have produced results contradictory to the worm-like chain model. Here we show that the free energy of a dsDNA loop as short as 60 bp in contour length can be well described by the wormlike chain model. We measured the breakage rates of small dsDNA loop stabilized by sticky ends using Fluorescence Resonance Energy Transfer (FRET). We found that the breakage rate vs. loop length relationship to be in good agreement with the worm-like chain model, but not with an alternative model which predicts superflexible behavior at short length scales. Furthermore, we found that energetics of dsDNA begins to deviate from the worm-like chain model below 60 bp. Our result pushes the lower limit of the worm-like chain regime of dsDNA down to 60 bp, and suggests that dsDNA undergoes structural transitions below this length.

1409-Pos Board B139
Polyethyleneimine-DNA Interactions
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Polyethyleneimine (PEI) is a cationic polymer with primary, secondary and tertiary amino groups separated by an ethylene bridge. PEI is available in both linear and branched forms, and many molecular weight forms are available commercially. PEI is amongst the first and very versatile transfection agents to deliver DNA to cells for gene targeted studies and therapeutic applications. By virtue of their cationic nature under physiologically compatible ionic and pH conditions, PEI can bind with DNA. Using total intensity and